Applicants have amended claims 1, 9, 14, 22, and 25 to further clarify the dermal lesions and dermonecrosis resulting from envenomation that may be treated or prevented by the methods of the present invention. Support for this is found in the specification on page 6, for example, lines 17-18. Applicants' invention is directed to any venom induced immune dysregulation, since immune stimulation by the IRM compound is the mode of action, which takes place, regardless of the venom or the envenomating organism. Accordingly, applicants respectfully request that the 35 U.S.C. § 112 rejection be withdrawn.

35 U.S.C. § 103 Rejections

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomai et al. (WO 98/17279) and Gerster et al. (U.S. Patent No. 6,110,929) in view of Bitterman-Deutsch et al. (HAREFUAH, 1990; 119(5-6):137-139), Mosbech et al. (Ugeskrift for Laeger, 1991:153(44):3067-3071), Binder (Medical Toxicology and Adverse Drug Experience, 1989;4(3):163-173), and Auerbach et al. (Journal of Emergency Medicine, 1987:5(6):487-491).

The Examiner's grounds for this rejection appear to be based on the following reason:

1. Tomai et al. and Gerster et al. teach imidazoquinoline amine and thiazoloquinolin amine compounds.
2. Tomai et al. teach that by inhibiting the activties of T-cell Type-2, these compounds reduce the production of cytokines such as interleukin-3, interleukin-4, and interleukin-5, reduce the production of IgE, and suppress eosinophils.
3. Reduced production of IgE and suppression of eosinophils is known for treatment of envenomation.

Applicants respectfully submit that the references relied upon taken together or in any combination do not support the obviousness rejection. None of the references or combinations thereof provide a suggestion or motivation to use the immune response modifier compounds according to the claimed invention, since, among other reasons, it is not established by these references, that by inhibiting T-cell Type-2 activities, reducing the production of cytokines, reducing the production of IgE, and suppression of eosinophils useful treatment of dermal lesions or prevention of dermonecroses caused by venom induced immune dysregulation was affected.

On the contrary, because the immune response modifier compounds are potent immune stimulants, one would not expect that these compounds put to the use of treating dermal lesions or

prevention of dermonecroses caused by venom induced immune dysregulation would be found to be highly effective. This is because in venom induced immune dysregulation, the immune system has already been stimulated by the venom, causing injury to the envenomated tissue, and further stimulation would be expected to worsen the condition.

The immune response modifier compounds have multiple effects on the immune response. Even though some cytokines are inhibited (e.g., IL-4, IL-5); many are up regulated (e.g., IFN, IL-1, IL-6). Even if it were clearly established by the references that down regulation of T-cell Type-2 activity would necessarily alleviate venom induced immune dysregulation, there still could not be a reasonable expectation of the found success in using the immune response modifier compounds according to the invention because of the complexity of the response of the immune system to the compounds.

The reported use of dapsone by Bitterman-Deutsch et al. could not provide a reasonable expectation of success at the time the invention was made, since dapsone is a completely different compound than the immune response modifier compounds used in the claimed invention. One could not predict that the claimed compounds, which elicit a completely different immune response, would be useful in the same manner as dapsone

In addition, there is no known or suggested use of or motivation to use the immune response modifier compounds for blocking chemotaxis in the relied upon references.

In summary, given that the immune response modifier compounds are potent immune stimulants, that in venom induced immune dysregulation the immune system has already been stimulated, and that the immune response modifier compounds have multiple effects on the immune response, a reasonable expectation of success is absent in the relied upon art for their use in the claimed invention.

Based on the foregoing, it is submitted that the application is in condition for allowance. Withdrawal of the rejections under 35 U.S.C. 112 and 103 is requested. Examination and reconsideration of the claims are requested. Allowance of the claims at an early date is solicited.

The Examiner is invited to contact Applicants' patent agent if the Examiner believes any remaining questions or issues could be resolved by doing so.

Respectfully submitted,

5-2-02
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**Version With Markings to Show Changes Made**

12. (once amended) A method of treating dermal lesions caused by [envenomation]venom induced immune dysregulation, the method comprising applying a therapeutically effective amount of an immune response modifier compound selected from the group consisting of imidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, imidazonaphthyridine amines, tetrahydroimidazonaphthyridine amines, oxazolopyridines amines, oxazoloquinoline amines, thiazolopyridine amines, thiazoloquinoline amines and 1,2-bridged imidazoquinoline amines to the site of the lesion.

9. (once amended) The method of claim 1 wherein the source of the [envenomation]venom induced immune dysregulation is an arthopod.

15. (once amended) A method of preventing dermonecrosis caused by [envenomation] venom induced immune dysregulation, the method comprising applying a therapeutically effective amount of an immune response modifier compound selected from the group consisting of imidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, imidazonaphthyridine amines, tetrahydroimidazonaphthyridine amines, oxazolopyridines amines, oxazoloquinoline amines, thiazolopyridine amines, thiazoloquinoline amines and 1,2-bridged imidazoquinoline amines to the site of the venom induced immune dysregulation.

22. (once amended) The method of claim 14 wherein the source of the [envenomation]venom induced immune dysregulation is an arthopod.

25. (once amended) The method of claim 14 wherein the source of the [envenomation]venom induced immune dysregulation is a marine animal.